BIOTECHNOLOGY

ORYZON GENOMICS

BUY

TARGET PRICE : 12,6€ (vs 3,1€) +314%

UPDATE REPORT + COMPANY CONTACT

2 FRANCHISES THAT COULD WELL HAVE SYNERGIES

Since the beginning of February, the company has entered an extremely buoyant Momentum. Several extrinsic and intrinsic factors have likely contributed to this rally, but the main explanation, in our opinion, remains the fact that the potential of vafidemstat in the treatment of neuropsychiatric disorders is strengthening and is increasingly revealed, account the clinical evidence provided by Oryzon Genomics, in parallel with competition which, for its part, is diminishing due to the lack of clinical success. In order to consider the changing landscape, political incentives in the field of neurological disorders, the strategy emerging among large pharmaceutical groups and the privileged position that Oryzon Genomics now occupies on the M&A chessboard, we have overhauled our valuation model. Based on our new assumptions, this results in a TP of €12.6 vs. €3.1 previously, with a Buy recommendation that we reiterate.

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Mid-term strategy focused on value creation

Oryzon Genomics' strategy focuses on mid-term value creation. Aware of the challenges surrounding neuropsychiatric disorders, the company wishes to prioritize its program with vafidemstat in BPD (borderline personality disorder). We believe this is the most valuable asset given its stage of development and addressable market potential. At the same time, the company is continuing to advance its oncology franchise, with most of clinical trials currently supported by academic partners in the US. This offers the dual advantage of minimizing clinical costs while maximizing visibility thanks to the partners' reputation.

Planned sell-Off of iadademstat to promote BD and even M&A

One of Oryzon Genomics' mid-term objectives is to advance the development of iadademstat in several oncology indications to clinical PoC (proof of concept). Upon reaching this milestone, the objective would be to monetize iadademstat through a sale of the asset. The proceeds from the sale (ISe: potential amount of €450 million) would secure the development of vafidemstat in the CNS franchise until the final results in the BPD potentially expected in 2029. Based on positive results, this could trigger a GO from a pharmaceutical player for a licensing agreement at the Ph III or regulatory stage or even promote a takeover.

Redesign of our valuation model and changes to assumptions

To consider the changing landscape and Oryzon Genomics' mid-term strategy, we have revised our model, which incorporates the signing of an agreement for a license or asset acquisition in 2027 for iadademstat in oncology, and a licensing agreement for vafidemstat by 2029 after the publication of the final Ph III results.

Buy opinion, TP revised to €12.60 vs. €3.10 previously

This revised TP reflects Oryzon Genomics' strategy and also takes into account recent developments in the landscape to integrate strengthening M&A opportunities. Our TP offers an upside of nearly +300%, justifying our renewed Buy opinion.

Invest Securities and the issuer have signed an analysis services agreement. 1/29

in € / share	2024e	2025e	2026e
Adjusted EPS	-0,06	-0,04	-0,04
chg.	*n.s.*	*n.s.*	*n.s.*
estimates chg.	*+26,8%*	*-0,2%*	*-0,2%*

au 31/12	2024e	2025e	2026e
PE	n.s.	n.s.	n.s.
EV/Sales	n.s.	n.s.	n.s.
EV/Adjusted EBITDA	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.
FCF yield*	n.s.	n.s.	n.s.
Div. Yield	n.s.	n.s.	n.s.

* After tax op. FCF before WCR

key points		
Closing share price	24/03/2025	3,0
Number of Shares (m)		65,8
Market cap. (€m)		200
Free float (€m)		166
ISIN		ES0167733015
Ticker		ORY-ES
DJ Sector		Health Technology

	1m	3m	Ytd
Absolute perf.	-12,5%	+100,6%	+117,5%
Relative perf.	-11,9%	+79,9%	+96,6%

Source : Factset, Invest Securities estimates

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SUMMARY

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Epigenetics at the service of precision medicine: LSD1 inhibitors

Oryzon Genomics is a company specializing in personalized medicine using the epigenetics approach to address various pathologies. Epigenetics refers to functional modifications of the genome that do not involve changes in the DNA sequence. These modifications occur in cellular metabolism as a fundamental regulatory mechanism to control the conformational transition between transcriptionally active and inactive states of chromatin. In fact, epigenetics makes it possible to regulate/modulate DNA and therefore the genes that will be available for expression in the cell. Overexpression or, on the contrary, the absence of expression of a gene, can be the cause of various pathologies, or promote their expression. Acting on the molecules involved in these epigenetic mechanisms is an approach that may have the potential to target certain diseases.

Oryzon Genomics has developed a platform from which two drug candidates have reached the clinical stage. The fundamental approach on which Oryzon has built its therapeutic strategy is to address the underlying causes of various diseases by targeting lysine-specific demethylase 1 (LSD1). This is a histone-modifying enzyme involved in regulating the expression of many genes important in the onset and progression of diseases such as cancer and central nervous system disorders. It is precisely in these two areas that the company has developed its current clinical pipeline. Specifically, Oryzon Genomics currently has a pipeline organized into two franchises, each based on a selective LSD1 inhibitor (LSD1i) active that has reached the Ph II stage:

- Iadademstat, evaluated in the field of oncology, in both liquid cancers and solid tumors;
- Vafidemstat is primarily used for the treatment of neuropsychiatric disorders.

In addition, other drug candidates have been selected and are currently undergoing preclinical development: ORY-3001 in sickle cell disease, and ORY-4001, a selective HDAC6 inhibitor, for ALS (amyotrophic lateral sclerosis) and CMT (Charcot Marie-Tooth disease).

Oryzon Genomics' pipeline

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)
			Phase Ia	Phase Ib	Phase IIa	Phase IIb		
CNS: Vafidemstat (ORY-2001) – CNS optimized LSD1 inhibitor								
Borderline personality disorder Agitation / Aggression & Overall Improvement	PORTICO						**Completed.** Study has results	Final Data 3Q24 ECNP-2024 EoP2 FDA meeting 3Q24 Ph III protocol submission 1H25 ★
Schizophrenia Negative Symptoms	EVOLUTION						**Recruiting**	Timeline updates in 2025
Kabuki Syndrome	HOPE			Phase Ib/II			**IND in evaluation**	IND in 2025 (subject to additional resources)
Oncology: Iadademstat (ORY-1001) – Selective LSD1 inhibitor								
AML 1L Unfit Patients Combination with azacitidine	ALICE						**Completed** Study has results	Final positive results published May 2024 (Lancet Haematology)
AML 1L Unfit Patients Combination with azacitidine and venetoclax	ALICE-2 (IIS-X002)			Phase Ib			**Recruiting** Sponsor: OHSU	1st cohort dosed
AML 1L Unfit Patients Combination with azacitidine and venetoclax	ALICE-3 (CRADA-AML)			Phase Ib			**Recruiting** Sponsor: NCI, Led by UPMC	1st patient dosed
AML R/R-Flt3mut+ Combination with gilteritinib	FRIDA			Phase Ib			**Recruiting**	Initial data presented at EHA-2024 Next data update EHA-2025 ★
MDS Combination with azacitidine	IIS-X005			Phase I			**Recruiting** Sponsor: MCW	1st patient dosed
Neuroendocrine High Grade R/R Combination with paclitaxel	C-X001 NET Basket						**Recruiting** Collab Study with FCCC	Study Updates 1H25
ED-SCLC 1L Combination with ICI	STELLAR-0 (CRADA-SCLC)				Phase I/II		**IND Approved** Sponsor: NCI, Led by MSKCC	FPI 1Q25
ED-SCLC 1L Combination with ICI	STELLAR				Phase II pivotal		**In preparation**(*) Company sponsored	IND 2025
Other Programs								
ORY-3001 (LSD1i) Sickle Cell Disease							IND enabling tox completed	
ORY-4001 (HDAC6i) CMT, ALS							IND enabling tox ongoing	

Source: Oryzon Genomics

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Oryzon's strategy: optimizing costs to accelerate value creation

Oryzon Genomics has worked to develop its two franchises in parallel, notably through collaborations with renowned academic teams in their fields of expertise. This is particularly the case in the field of oncology where several collaborations are active with the support (human, material and financial resources) of several institutions in the US: the NCI (National Cancer Institute), the OHSU (Oregon Health & Science University), the MCW (Medical College of Wisconsin) and the FCCC (Fox Chase Cancer Center). Apart from the Ph Ib FRIDA trial in AML (acute myeloid leukemia) and the Ph II STELLAR trial currently in preparation in the field of SCLC (small cell lung cancer) in first-line in combination with ICI (checkpoint inhibitors), all other oncology programs are sponsored by academic teams. This collaborative strategy allows Oryzon Genomics to advance its programs with expert teams at reduced costs, with the majority of costs being borne by the academic teams. In addition to reduced costs, this approach brings other benefits to Oryzon Genomics:

- Patient access: With medical teams working at renowned institutes in the US, patient recruitment is facilitated due to the presence of patients in hospital departments. Consistently, medical teams conducting their own clinical trials launch programs aimed at identifying technologies capable of treating the patient populations they monitor.
- Recognition: The increasing number of collaborations with various medical teams is a strong signal of the experts' acceptance of the technologies developed by Oryzon Genomics. With no fewer than five active collaborations in the US in the field of oncology, this underscores the robustness of the rationale for the LSD1 inhibitor approach in oncology, and the therapeutic potential offered by iadademstat, according to the medical community.
- Visibility: The communication of the work conducted by these various teams, both at conferences and in medical journals, should help shed light on the potential of this approach. As pharmaceutical companies are also present at major medical meetings, the presentations of data obtained as part of the work carried out by these different teams should contribute to increasing awareness of this class of assets among pharmaceutical companies.

Although Oryzon Genomics has primarily focused on its oncology franchise in recent years, recent advances in the field of CNS (Central Nervous System) disorders have led to a fairly clear shift in the company's priorities. Indeed, the results published on January 5, 2024 in the field of borderline personality disorder (BPD) now suggest significant medium-term potential in this area. In a note published in January 2025, we mentioned our feeling of a reprioritization of the BPD program, and a relegation of the oncology franchise, which nevertheless continues to progress through collaborations. This feeling is now reinforced by the strategy that Oryzon Genomics wishes to deploy, which consists of optimizing costs in order to target value creation. From an economic perspective, given that the CNS field offers greater potential than cancer, given the size of the target markets, the momentum in each therapeutic area, the stages of progress of the programs, and the likelihood of success, it was only natural for Oryzon to prioritize the BPD program. At this stage, the company's strategic objective is to allocate the majority of its resources to the development of the BPD program:

- Preparation of a Ph III in BPD, which could be initiated by the end of 2025 if the FDA validates the protocol, which will be submitted in H1 25, and grants authorization to initiate the trial in H2 25.
- Continue creating value in oncology by minimizing R&D costs while maximizing the franchise's potential by achieving clinical proof of concept in several niche indications simultaneously.

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Two independent franchises that may interest different acquirers

Oryzon Genomics is no exception in the Biotech segment, and like most biotechnology companies, the group is deploying a strategy that targets agreements with industrial partners at key stages of its clinical development. While licensing agreements are among the top options for strategic transactions targeted by Oryzon Genomics, M&A is also among the opportunities being considered. However, the fields of oncology and CNS disorders are rarely invested in by the same groups (with a few exceptions among the Top 10 groups), which we believe may limit the chances of an acquisition and internalization of all Oryzon Genomics technologies via a takeover bid. Since cancer and neuropsychiatric disorders are very different, we believe it is more likely that each product will be the subject of an agreement with a separate partner.

After discussions with the company, we were confirmed that one of the options being considered for the group's strategic development was the monetization of the iadademstat product within two to three years, once the ongoing Phase II trials have been completed. The strategic objective of such a transaction would be twofold:

- Significantly strengthen cash flow through the proceeds from the sale of iadademstat to a third party, and achieve financial independence to achieve development objectives in the CNS franchise;
- Become a pure CNS player following the sale of iadademstat in oncology, which should significantly increase the company's chances of becoming an M&A target for a pharmaceutical group active in the field of neuropsychiatric disorders.

Programs mainly sponsored by academic teams (excluding ALICE, FRIDA and STELLAR)

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)
			Phase Ia	Phase Ib	Phase IIa	Phase IIb		
Oncology: Iadademstat (ORY-1001) – Selective LSD1 inhibitor								
AML 1L Unfit Patients Combination with azacitidine	ALICE						Completed Study has results	Final positive results published May 2024 (Lancet Haematology)
AML 1L Unfit Patients Combination with azacitidine and venetoclax	ALICE-2 (IIS-X002)			Phase Ib			Recruiting Sponsor: OHSU	1st cohort dosed
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AML R/R-Flt3mut+ Combination with gilteritinib	FRIDA			Phase Ib			Recruiting	Initial data presented at EHA-2024 Next data update EHA-2025 ★
MDS Combination with azacitidine	IIS-X005			Phase I			Recruiting Sponsor: MCW	1st patient dosed
Neuroendocrine High Grade R/R Combination with paclitaxel	C-X001 NET Basket						Recruiting Collab Study with FCCC	Study Updates 1H25
ED-SCLC 1L Combination with ICI	STELLAR-0 (CRADA-SCLC)				Phase I/II		IND Approved Sponsor: NCI, Led by MSKCC	FPI 1Q25
ED-SCLC 1L Combination with ICI	STELLAR				Phase II pivotal		In preparation(*) Company sponsored	IND 2025

Transfer rights to Iadademstat to finance programs with Vafidemstat

$$

What level of amount can to possibly expect ?

100% proprietary Oryzon Genomics programs

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)
			Phase Ia	Phase Ib	Phase IIa	Phase IIb		
CNS: Vafidemstat (ORY-2001) – CNS optimized LSD1 inhibitor								
Borderline personality disorder Agitation / Aggression & Overall Improvement	PORTICO						Completed. Study has results	Final Data 3Q24 ECNP-2024 EoP2 FDA meeting 3Q24 Ph III protocol submission 1H25 ★
Schizophrenia Negative Symptoms	EVOLUTION						Recruiting	Timeline updates in 2025
Kabuki Syndrome	HOPE			Phase Ib/II			IND in evaluation	IND in 2025 (subject to additional resources)
ORY-4001 (HDAC6i) CMT, ALS							IND enabling tox ongoing	

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In our view, separating the Cancer and CNS franchises could prove to be a virtuous strategy that would emphasize value creation for Oryzon Genomics and its shareholders. Given the evolving landscape in each of its franchises, and the clinical results achieved to date by Oryzon Genomics, we reiterate our view that the bulk of Oryzon Genomics' value currently lies in its BPD program. The plan, which would consist of divesting iadademstat in the short/mid-term in order to allocate the funds generated by the transaction to accelerate the development of vafidemstat in CNS disorders, is the most opportune, in our view. This scenario is further supported by the dynamics in each area:

- Oncology: The sector is highly competitive, with the majority of clinical trials being conducted in this area. Indeed, it is the most invested market in the pharmaceutical industry, which could provide Oryzon Genomics with a privileged position for "opportunistic" outlicensing. In this scenario, the acquisition price for the rights to the target technology would be in a mid-range.
- CNS disorders: The sector has the advantage of low competition versus a very high medical need, which could provide a prime position for strategic M&A. In this type of scenario, the acquisition price could be relatively high.

LSD1 inhibitor product pipeline in oncology

All Financial Data in US $ (mln)

Rank	Product	Generic Name	Company	Therapeutic Subcategory	Patent Expiry	Annual Sales WW - Sales 2024	2030	CAGR	Total Change	F (Sales)	WW Phase (Current)	Company Product Name
1	Bomedemstat	bomedemstat	Merck & Co	Other cancer treatments	déc. 2036	-	58	n/a	58	F	Phase III	Bomedemstat
2	Iadademstat	iadademstat	Oryzon Genomics	Other cancer treatments		-	26	n/a	26	F	Phase II	Iadademstat
-	Second Generation LSD1 Research Program	-	Salarius Pharmaceuticals	Other anti-cancers	-	-	-	-	-		Pre-clinical	Second Generation LSD1 Research Program
-	LSD1 Research Program	-	EpiAxis Therapeutics	Other cancer treatments	-	-	-	-	-		Pre-clinical	LSD1 Research Program
-	EXS-74539	-	Exscientia	Other cancer treatments	-	-	-	-	-		Transferred (M&A) - Pre-clinical	EXS74539
Total						-	84	n/a	84			

Source: Evaluate Pharma

To date, two LSD1 inhibitor products are being developed in oncology clinical trials: iadademstat from Oryzon Genomics and bomedemstat from Merck & Co. While Oryzon Genomics is developing a proprietary product, Merck acquired bomedemstat through the acquisition of Imago BioSciences in 2023 for a total consideration of nearly $1.36 billion. We have two other M&A transactions involving an LSD1 inhibitor asset:

- CPI-482: This product was initially developed by Constellation Pharmaceuticals before its acquisition in 2021 by MorphoSys, which was itself acquired by Novartis in 2024. Since then, work in the field of AML has been abandoned and has not progressed beyond the preclinical stage.
- CC-90011: This LSD1 inhibitor is in the pipeline of BMS, which acquired it in 2019 through the acquisition of blood cancer specialist Celgene (Revlimid) for the tidy sum of $74 billion. Work on AML has also been abandoned.

Buyout transactions involving an LSD1 inhibitor

Date of Acquisition	Company	Strategy	Acquired Company	Product	Indication Summary
17/05/2024	Novartis	Company acquisition	MorphoSys	CPI-482	Leukaemia, acute myeloid (AML) [Abandoned - Pre-clinical]
11/01/2023	Merck & Co	Company acquisition	Imago BioSciences	Bomedemstat	Polycythaemia vera [Phase III]; Myelofibrosis [Phase III]; Thrombocythaemia [Phase III]; Leukaemia, acute myeloid (AML) [Phase II]; Small cell lung cancer (SCLC) [Phase II]; Myelodysplastic syndrome (MDS) [Phase I]; Solid tumour indications [Abandoned - Research project]
02/06/2021	MorphoSys	Company acquisition	Constellation Pharmaceuticals	CPI-482	Leukaemia, acute myeloid (AML) [Transferred (M&A) - Pre-clinical]
20/11/2019	Bristol Myers Squibb	Company acquisition	Celgene	CC-90011	Small cell lung cancer (SCLC) [Phase II]; Solid tumour indications [Phase II]; Non-Hodgkin lymphoma (NHL) [Phase I]; Prostate cancer [Abandoned - Phase I]; Leukaemia, acute myeloid (AML) [Abandoned - Phase I]; General cancer indications [Abandoned - Research project]

Source: Evaluate Pharma

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These transactions illustrate the interest shown by certain groups in this oncology asset class in recent years. LSD1 inhibitors have been the subject of other transactions, including licensing agreements at various stages.
These transactions are interesting on two levels:

- They constitute a benchmark for assessing the potential value of a future transaction for Oryzon Genomics' iadademstat,
- They fuel news flow for this asset class and provide benchmark catalysts offering a potentially favorable read-across for iadademstat.

License agreements involving an LSD1 inhibitor in oncology

	Deal Date	Product	Company	Deal Partner	Deal Value ($m)	Upfront Cash ($m)	Maximum Royalty (%)	Status on Deal Date	WW Phase (Current)	Product Specific Development Milestones ($m)	Product Specific Sales Milestones ($m)	Deal Source Link
Acquisition - Product	02/06/2021	CPI-482	MorphoSys	Royalty Pharma	2 025	1 425	-	-	Transferred (M&A) - Pre-clinical	-	-	Source
Licensing - Product	18/03/2015	RASP-201	Actavia Life Sciences	Istituto Europeo di Oncologia	-	-	-	Research project	Pre-clinical	-	-	
	07/04/2014	Iadademstat	Roche	Oryzon Genomics	521	21	-	Phase I	Abandoned - Phase I	-	-	Source
Total					**521**	**21**	-			**0**	**0**	
Licensing - Services	02/08/2022	Seclidemstat	Salarius Pharmaceuticals	VolitionRX	-	-	-	-	Phase II	-	-	Source
Report Total					**2 546**	**1 446**	-			**0**	**0**	

	Deal Date	Company	Deal Type	Product	Deal Partner/ Product Source	Status on Deal Date	Upfront Payment ($m)	Deal Value ($m)
Active	16/12/2015	EpiAxis Therapeutics	In-licensed	EPI-111	University of Canberra	Pre-clinical	-	-
	18/03/2015	Actavia Life Sciences	In-licensed	RASP-201	Istituto Europeo di Oncologia	Research project	-	-
	-	TES Pharma	In-licensed	RASP-201	Actavia Life Sciences	Pre-clinical	-	-
Inactive	07/04/2014	Roche	In-licensed	Iadademstat	Oryzon Genomics	-	21	521
	-	Undisclosed Partner Sales	In-licensed	Iadademstat	Oryzon Genomics	-	-	-
	-	Undisclosed Partner Sales	In-licensed	Bomedemstat	Imago BioSciences	Phase III	-	-

Source: Evaluate Pharma

Furthermore, in the LSD1i (LDS1 inhibitor) pipeline, the asset that most directly compares to iadademstat is bomedemstat:

- Similar development stage: Ph III for bomedemstat vs. Ph II for iadademstat. The other LSD1i assets have not advanced beyond the preclinical stage.
- Target indications: Several indications in the field of liquid cancers and also solid tumors are being explored, including AML and SCLC, which are common to both iadademstat and bomedemstat.
- Company profile: When it was acquired by Merck & Co., Imago was a biotech company that had just been listed on the Nasdaq market. It was a single-product company developing bomedemstat as a monotherapy or in combination in several indications of cancers and rare hematological diseases.

Imago BioSciences' pipeline

Source: Imago BioSciences - Dossier d'enregistrement SEC. Juin 2021

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A proposed sell-off of Oryzon Genomics' oncology franchise could be favored in the short term by the news flow expected by competitors, notably Merck & Co. Indeed, Ph III results are expected in 2027 in essential thrombocytopenia, a rare chronic blood disease. This is the most common myeloproliferative neoplasia, most often caused by genetic mutations that lead to excessive production of platelets by the bone marrow, which can obstruct blood flow and cause a stroke, a heart attack, or a pulmonary embolism. Epidemiological data estimate that fewer than 200,000 people in the US are affected by this pathology. Results from a 300-patient randomized, double-blind, controlled Ph III study evaluating the benefit of bomedemstat vs. hydroxyurea in terms of sustained clinicohematological response in treatment-naïve patients with essential thrombocythemia are expected in mid-2027. If successful, this could create favorable momentum for the LSD1i asset class. The prospect of regulatory approval in a niche oncology market could attract interest from other oncology players for an acquisition, as bomedemstat is also being evaluated in several other indications.

Clinical programs involving bomedemstat

	Study Title	Study Start	Phase	Status	Sponsor	Conditions	Interventions	Study Type	NCT Number	Study Completion	Primary Completion
1	Drug-Drug Interaction Study of **Bomedemstat** and Carbamazepine in Healthy Adult Participants (MK-3543-020)	2024-10-02	Phase 1	Completed	Merck Sharp & Dohme LLC	• Healthy	• Drug: **bomedemstat** • Drug: carbamazepine	Interventional	NCT06596668	2025-03-11	2025-02-05
2	**Bomedemstat** vs Hydroxyurea for Essential Thrombocythemia (MK-3543-007)	2024-07-16	Phase 3	Recruiting	Merck Sharp & Dohme LLC	• Essential Thrombocythemia	• Drug: **Bomedemstat** • Drug: Hydroxyurea • Drug: **Bomedemstat** placebo • 1 more	Interventional	NCT06456346	2029-04-15	2027-04-15
3	A Study to Evaluate Safety and Efficacy of **Bomedemstat** (MK-3543-017)	2024-05-23	Phase 3	Recruiting	Merck Sharp & Dohme LLC	• Thrombocythemia, Essential • Primary Myelofibrosis • Myelofibrosis • 3 more	• Drug: **Bomedemstat**	Interventional	NCT06351631	2034-12-04	2034-12-04
4	A Study of **Bomedemstat** (IMG-7289/MK-3543) Compared to Best Available Therapy (BAT) in Participants With Essential Thrombocythemia and an Inadequate Response or Intolerance of Hydroxyurea (MK-3543-006)	2023-12-31	Phase 3	Recruiting	Merck Sharp & Dohme LLC	• Essential Thrombocythemia	• Drug: **Bomedemstat** • Drug: Anagrelide • Drug: Busulfan • 2 more	Interventional	NCT06079879	2028-08-18	2026-08-18
5	Venetoclax and **Bomedemstat** in Patients with Relapsed/Refractory Acute Myeloid Leukemia	2022-11-19	Phase 1	Suspended	Terrence J Bradley, MD	• Acute Myeloid Leukemia • Refractory Acute Myeloid Leukemia • Acute Myeloid Leukemia, in Relapse	• Drug: **Bomedemstat** • Drug: Venetoclax	Interventional	NCT05597306	2025-11-19	2025-11-19
6	**Bomedemstat** (IMG-7289) Plus Ruxolitinib for Myelofibrosis	2022-12-01	Phase 2	Recruiting	The University of Hong Kong	• Myelofibrosis	• Drug: **Bomedemstat**	Interventional	NCT05569538	2025-12-31	2024-12-31
7	A Study of **Bomedemstat** (MK-3543) in Participants With Polycythemia Vera (MK-3543-004)	2023-09-07	Phase 2	Active, not recruiting	Imago BioSciences, Inc., a subsidiary of Merck & Co., Inc., (Rahway, New Jersey USA)	• Polycythemia Vera	• Drug: **Bomedemstat**	Interventional	NCT05558696	2025-03-24	2025-03-24
8	Extension Study of **Bomedemstat** (IMG-7289/MK-3543) in Participants With Myeloproliferative Neoplasms (IMG-7289-CTP-202/MK-3543-005)	2021-12-16	Phase 2	Completed	Imago BioSciences, Inc., a subsidiary of Merck & Co., Inc., (Rahway, New Jersey USA)	• Thrombocythemia, Essential • Primary Myelofibrosis	• Drug: **Bomedemstat**	Interventional	NCT05223920	2024-08-22	2024-08-22
9	**Bomedemstat** and Maintenance Immunotherapy for Treatment of Newly Diagnosed Extensive Stage Small Cell Lung Cancer	2022-04-11	Phase 1 Phase 2	Terminated WITH RESULTS	University of Washington	• Extensive Stage Lung Small Cell Carcinoma • Limited Stage Lung Small Cell Carcinoma	• Drug: **Bomedemstat** • Biological: Atezolizumab	Interventional	NCT05191797	2024-04-05	2023-08-03
10	Study of **Bomedemstat** in Participants With Essential Thrombocythemia (IMG-7289-CTP-201/MK-3543-003)	2020-09-08	Phase 2	Completed WITH RESULTS	Imago BioSciences, Inc., a subsidiary of Merck & Co., Inc., (Rahway, New Jersey USA)	• Essential Thrombocythemia	• Drug: **Bomedemstat**	Interventional	NCT04254978	2023-03-23	2023-03-23
11	**Bomedemstat** (IMG-7289/MK-3543) in Participants With Myelofibrosis (IMG-7289-CTP-102/MK-3543-002)	2017-07-18	Phase 1 Phase 2	Completed WITH RESULTS	Imago BioSciences, Inc., a subsidiary of Merck & Co., Inc., (Rahway, New Jersey USA)	• Myelofibrosis • Post-polycythemia Vera Myelofibrosis (PPV-MF) • Post-essential Thrombocythemia Myelofibrosis (PET-MF) • 1 more	• Drug: **Bomedemstat**	Interventional	NCT03136185	2022-03-08	2022-03-08
12	A Study of **Bomedemstat** (IMG-7289/MK-3543) With and Without ATRA, in Participants With Advanced Myeloid Malignancies (IMG-7289-CTP-101/MK-3543-001)	2016-10-06	Phase 1 Phase 2	Completed WITH RESULTS	Imago BioSciences, Inc., a subsidiary of Merck & Co., Inc., (Rahway, New Jersey USA)	• Acute Myeloid Leukemia • Myelodysplastic Syndrome	• Drug: **bomedemstat** • Drug: tretinoin	Interventional	NCT02842827	2018-10-30	2018-10-30

Source: Clinicaltrials.gov

As for Oryzon Genomics, the strategy for iadademstat is to advance developments, particularly through active collaborations, to achieve clinical proof of concept in various oncology indications. In the coming months, several Ph I and Ph II clinical trial results are expected.

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By the time bomedemstat's Ph III results are published in mid-2027, most of the programs currently evaluating iadademstat's potential will have delivered clinical results, which should favor the conditions for a potential sell-off. Oryzon Genomics' development plan for iadademstat is to consolidate the clinical evidence supporting the use of its LSD1i vs. standard treatments in indications with unmet medical need.

Clinical programs involving iadademstat

Study Title	Study Start	Phase	Status	Sponsor	Conditions	Interventions	Study Type	NCT Number	Study Completion	Primary Completion
A Randomized Study of ASTX727 With or Without **iadademstat** in Advanced Myeloproliferative Neoplasms (MPNs) New	2025-05-09	Phase 2	Not yet recruiting	National Cancer Institute (NCI)	• Accelerated Phase Myeloproliferative Neoplasm • Blast Phase Myeloproliferative Neoplasm • Essential Thrombocythemia • 5 more	• Procedure: Biospecimen Collection • Procedure: Bone Marrow Aspiration • Procedure: Bone Marrow Biopsy • 2 more	Interventional	NCT06661915	2027-06-01	2027-06-01
Testing the Combination of an Anti-Cancer Drug, **Iadademstat**, With Other Anti-Cancer Drugs (Venetoclax and Azacitidine) for Treating AML	2024-12-18	Phase 1	Suspended	National Cancer Institute (NCI)	• Acute Myeloid Leukemia	• Drug: Azacitidine • Procedure: Biospecimen Collection • Procedure: Bone Marrow Aspiration • 3 more	Interventional	NCT06514261	2026-09-16	2026-09-16
Iadademstat with Hypomethylating Agent in Patients with Myelodysplastic Syndrome	2025-01-10	Phase 1	Recruiting	Medical College of Wisconsin	• Myelodysplastic Syndromes	• Drug: Azacitidine Level -1 • Drug: Azacitidine Level 0 • Drug: Azacitidine Level 1 • 3 more	Interventional	NCT06502145	2027-10	2026-10
Iadademstat in Combination With Azacitidine and Venetoclax in Treating Newly Diagnosed Acute Myeloid Leukemia	2024-08-22	Phase 1	Recruiting	OHSU Knight Cancer Institute	• Acute Myeloid Leukemia • Myelodysplastic Syndrome/Acute Myeloid Leukemia	• Drug: Azacitidine • Procedure: Biospecimen Collection • Procedure: Bone Marrow Biopsy • 5 more	Interventional	NCT06357182	2026-05-29	2026-03-08
Testing the Combination of an Anti-cancer Drug, **Iadademstat**, With Other Anti-cancer Drugs (Atezolizumab or Durvalumab) at Improving Outcomes for Small Cell Lung Cancer	2025-08-17	Phase 1 Phase 2	Recruiting	National Cancer Institute (NCI)	• Extensive Stage Lung Small Cell Carcinoma • Stage IV Lung Cancer AJCC v8	• Biological: Atezolizumab • Procedure: Biopsy • Procedure: Biospecimen Collection • 6 more	Interventional	NCT06287775	2029-07-25	2029-07-25
Study of **Iadademstat** and Gilteritinib in Patients With R/R AML With FMS-like Tyrosine Kinase Mutation (FLT3 Mut+)	2022-11-14	Phase 1	Recruiting	Oryzon Genomics S.A.	• Acute Myeloid Leukemia, in Relapse • Acute Myeloid Leukemia Refractory	• Drug: **Iadademstat** • Drug: Gilteritinib Oral Tablet	Interventional	NCT05546580	2025-11-30	2025-11-30
Iadademstat in Combination With Paclitaxel in Relapsed/Refractory SCLC and Extrapulmonary High Grade NET	2022-12-21	Phase 2	Recruiting	Fox Chase Cancer Center	• Small-cell Lung Cancer • Neuroendocrine Carcinoma	• Drug: **Iadademstat** • Drug: Paclitaxel	Interventional	NCT05420636	2026-08-07	2025-08-05

Source: Clinicaltrials.gov

In the scenario of positive Ph III results for Merck & Co, we can imagine a reaction similar to that observed during the month of February for vafidemstat in CNS disorders. The highlighting of the potential of the LSD1i approach via the success of bomedemstat could strengthen the market interest in this asset class, and be a trigger for the positioning of an oncology player on iadademstat. Two types of transactions are possible:

1) **a licensing agreement**. We have few transactions in the LSD1i segment to estimate the amount of such an agreement. However, if we expand our field of oncology in rare liquid cancers, the amounts currently mobilized are in line with the terms of the agreement that was signed between Roche and Oryzon Genomics in April 2014. As a reminder, the agreement concerned iadademstat for an amount of up to $521 million, including $21 million of upfront paid upon signing the agreement. At the time, iadademstat was being evaluated in Ph I trials. Although Roche decided to extend the collaboration agreement, which was initially for 2 years, by 1 year, the group finally decided in July 2017 to end the collaboration and return the rights to iadademstat to Oryzon Genomics following an internal review of its candidate portfolio. Since then, Oryzon Genomics has advanced its programs by validating Ph I and Ph II trials, and by multiplying the target indications. However, given the changing landscape and M&A dynamics in the pharmaceutical industry (more competition, increasing number of transactions but at lower levels), we consider that the terms of the agreement with Roche are in line with what Oryzon Genomics could currently expect for iadademstat.
   A retrospective analysis of global M&A transactions between 1990 and 2024 by BCG shows that 2014, 2015, and 2021 saw relatively intense M&A activity. Unsurprisingly, 2020 was among the least active years of the 2014-2024 decade. From 2022 onward, M&A activity declined overall, both in volume and total deal size.

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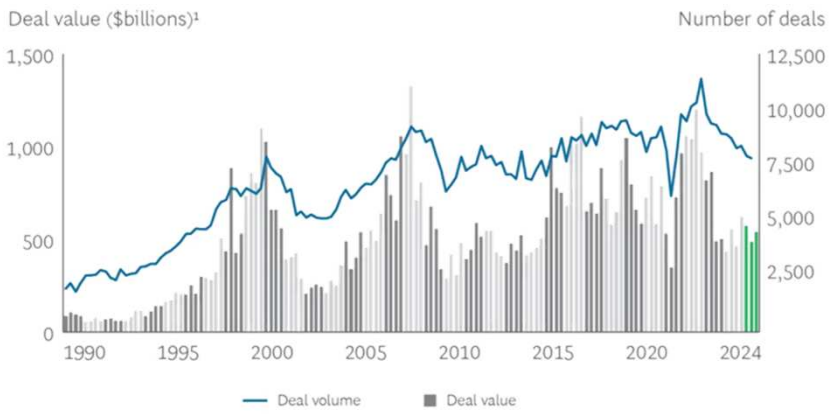
Evolution of global M&A activity



Source: Refinitiv, BCG

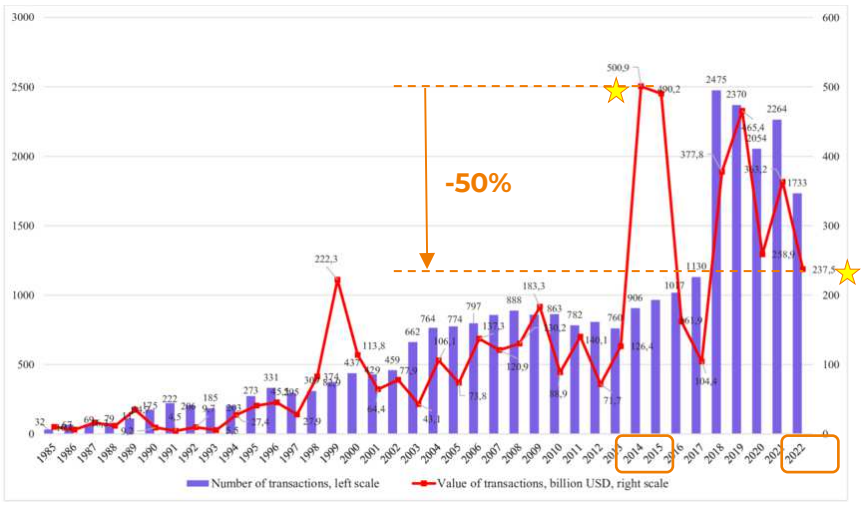
Specifically, regarding the healthcare sector, a study published in 2023 in the journal Economics and Education highlights the significant gap between the years 2024-2025 (the Oryzon/Roche deal was concluded in 2014) and more recent years. Furthermore, two key insights emerge from our analysis of the evolution of healthcare M&A activity:

i. The significant reduction in the overall value of transactions, with the level having declined by more than half between 2014, the historic peak, and 2022: $500.9 billion vs. $237.5 billion.

ii. Conversely, the sharp increase in transaction volume since 2018, which, alongside the decline in deal value, highlights the very sharp drop in value per transaction: an average of $553 million in 2014 vs. $137 million in 2022, a decline of 75%.

Taking this reality into account, we therefore estimate that the value of the deal signed in 2014 with Roche could broadly correspond to the value of a deal that would be signed at the current stage of iadademstat's programs. The progress of developments since this first agreement should generally offset the overall loss in transaction value that we have been witnessing in recent years in the healthcare sector.

Evolution of M&A activity in Healthcare



Source: Economics and Education 8(1):30-37. May 2023

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2) **an acquisition agreement**. The Imago/Merck & Co transaction is probably the most direct reference for estimating what a sale of iadademstat to a third party could represent. At the time of its acquisition, Imago was a single-product company developing bomedemstat in several oncology indications and whose flagship program had reached the Ph II stage. The transaction involved a total amount of nearly $1.36 billion, representing a premium of +107% compared to Imago BioSciences' pre-transaction market capitalization. If we apply the same ratios to Oryzon Genomics, this could represent an acquisition price of nearly €450 million, knowing that Oryzon's current value is based on two assets; iadademstat and vafidemstat. However, the clinical and regulatory validation of an LSD1i asset in the event of the success of bomedemstat, should significantly increase the valuation of LSD1i assets, which could justify an acquisition price of around €450m for iadademstat alone at the Ph II stage validated in several indications in hematology and in certain niche solid cancers.

Estimation of the agreement amount in the scenario of a iadademstat sell-off	
Imago maket capitalization before its acquisition	657 m$
Oryzon Genomics current market capitalization	218 m€
Ratio	3,014
Agreement amount for Imago's acquisition by Merck MSD	1,36 Md$
Estimated agreement for a sell-off of iadademstat over a 2-year horizon	451 m€

Source: Invest Securities

These are the estimates we used to assess the potential value of iadademstat in either of these two scenarios in our valuation model.

Although Oryzon Genomics remains open to all opportunities, the option of divesting iadademstat appears to be the most value-creating in the mid-term, as it should provide the company with the means to accelerate its clinical development in the CNS franchise and, under optimal conditions, reach major turning points within a five-year horizon:

- Net proceeds from the divestment of iadademstat estimated at around €450 million,
- Reaching the milestone of final Ph III results in BPD, paving the way for regulatory approval in the US and Europe. Beyond the success of the program, this should probably trigger the interest of a pharmaceutical player given the M&A dynamic in this segment for several years, which is reinforced by the activity of the title since the beginning of February 2025. We note that the title is very sought after, and that a major part of the flows come from the US, probably in view of the next stages in the program in the BPD.

Regarding the CNS franchise, Oryzon Genomics is mobilizing most of its resources to advance the BPD program to the Ph III stage. The group's strategy is to sign a license agreement as soon as possible. We believe that an agreement is most likely to be signed upon publication of the final Ph III results, which we anticipate by 2029 if the trial is initiated at the end of 2025. Indeed, given the clinical failure rate in the field of CNS disorders, it seems more likely that a player will wait for advanced clinical results before positioning itself in order to limit the risks of acquiring license rights for the development and commercialization of a product in this field. This is indeed the strategy that is increasingly being adopted by industry players who are prepared to commit very large amounts on the condition that the target assets have reached an advanced stage of maturity (Ph III validated or even obtaining regulatory approval) and/or that they are products addressing highly strategic therapeutic areas responding to a sectoral trend (e.g.: GLP-1).

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Achievements in BPD before the upcoming phase III milestone

On January 5, 2024, Oryzon Genomics published the topline results of its Ph IIb PORTICO trial in borderline personality disorder. Although they were negative on the 2 primary endpoints, the interesting fact is that all the parameters evaluated showed a positive trend in favor of vafidemstat vs. placebo (statistically significant value not reached). In addition, out of all 11 criteria evaluated, 2 were statistically significant on key aspects: the severity of BPD symptoms and the feeling of anger associated with aggression and agitation. Furthermore, an overall assessment of the study criteria by GST (global statistical test p-value, useful for evaluating the benefit of a potential treatment on a complex and multifactorial pathology) also confirmed a strong positive trend on all 11 study criteria in favor of vafidemstat treatment vs. placebo.

The final data were presented at the ECNP (European College of Neuropsychopharmacology) congress in September 2024. Compared to the topline results presented in early January 2024, the final results show an improvement in the measured scores, particularly on the two criteria that had emerged positive in the analysis. The reduction in patients' agitation and aggression measured by STAXI-2 emerged as statistically and clinically significant with a p value of 0.0071 during weeks 8 to 12 vs a p value of 0.0259 in the first analyses. The relative difference in this score between the test group and the placebo group reached a maximum of 92.1% at week 10 and a mean reduction of 58.6% during weeks 8 to 12. The second criterion that emerged positive, namely the BEST score which measures the global severity of the BPD group, also showed an improvement vs. preliminary data, with a p value of 0.0260 over weeks 8 to 12 (previously p = 0.0423). The maximum relative reduction in the vafidemstat group vs. placebo reached 38.9% at week 10, with a mean reduction of 30.9% during weeks 8 to 12. Other evaluation criteria among the 11 scores measured in total in this trial involving 211 patients showed an improvement in the p value without reaching statistical significance. Additionally, the results showed a trend toward improvement in depression as measured by the BDI-II total score over weeks 8 to 12 (p = 0.0944), with a relative reduction of around 42%. Finally, the overall trend toward improvement across all measured criteria (Global Statistical Test = GST) was confirmed in the final analysis with a statistically significant p value, particularly for overall improvement in disease severity and agitation/aggression (p = 0.0362 vs. a strong trend previously). As in all previous clinical studies, vafidemstat was shown to be safe and well tolerated.

The 2 primary endpoints (not met):

1. **Efficacy: Clinical Global Assessment Scale - Agitation/Aggression-Focused Severity (CGI-S A/A)**: Assessment of the difference on the Clinical Global Assessment Scale - Agitation/Aggression-Focused Severity (CGI-S A/A) between baseline and a specific week, between the active treatment group and the placebo group.
2. **Efficacy: Borderline Personality Disorder Checklist**: Assessment of the difference on the Borderline Personality Disorder Checklist between baseline and a specific week, between the active treatment group and the placebo group.

The 2 secondary endpoints (among 9 assessed) were positive:

1. **Efficacy: Assessment of BPD Severity Over Time (BEST)**: Assessment of the difference on the BEST scale between the active treatment group and the placebo group.
2. **Efficacy: State-Specific Anger Inventory (STAXI-2)**: Assessment of the difference on the STAXI-2 inventory between the active treatment group and the placebo group.

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Most clinical programs conducted in this area have failed to demonstrate efficacy for patients. In fact, there is currently no approved treatment for this complex condition. According to Oryzon Genomics, the PORTICO trial is the first study of this scale to demonstrate efficacy on two criteria. This is why the company has 25 and discussions with the FDA, which have proven positive. Conditions for which there is little clinical data and a relatively limited understanding of the mechanisms underlying the development of the disorder can benefit from careful listening by regulatory agencies, which can be more flexible and adaptable in terms of assessing clinical results. Indeed, we believe that in the absence of effective treatments to address this condition, the demonstration of a positive effect of vafidemstat on all the criteria evaluated, including two significantly improved ones, is an opportunity for patients that regulatory agencies must consider, especially for a product whose safety profile appears generally satisfactory.

According to KOLs (key opinion leaders), a clinically effective product in BPD would be a drug candidate capable of achieving an improvement of at least 25% on the evaluated criteria. In this register, vafidemstat showed an average improvement of 30.9% during weeks 8 to 12 of treatment for the BEST criterion (measurement of the severity of BPD symptoms and appropriate responses), and an average reduction of 58.6% for the STAXI-2 Trait Anger criterion (anger and aggression/agitation) with a p value of 0.0071. The company also conducted a biomarker analysis of PORTICO data to identify patient profiles that would be more likely to respond favorably to vafidemstat treatment. If a correlation is demonstrated between the biomarker level and clinical response, this will also be submitted to the FDA to allow patient segmentation and selection of best responders for recruitment for the Ph III trial currently in preparation.

On March 3, 2025, the company announced that it had established the endpoints that will serve as primary and secondary objectives in its pivotal Ph III trial. These parameters were defined in collaboration with ORYZON's new Clinical Advisory Board (CAB), composed of leading international experts in psychiatric research and clinical trials on psychiatric disorders. The participation of these experts is crucial to ensure the relevance and robustness of the design and protocol of the clinical trial that will be submitted to the FDA for review in H1 25. The CAB, through its expertise, notably helped ensure that the protocol complies with clinical field requirements, and therefore with FDA standards, by integrating well-validated and widely recognized assessment scales for measuring agitation and aggression in BPD patients. At the EOP2 (end of Ph II) meeting, the FDA provided generally positive feedback 25 and indicated that the primary endpoint of the Ph III trial could be the STAXI-2 score to measure illness-related anger, as agitation and aggression in BPD could be recognized as a therapeutic indication. Secondary endpoints should include both patient- and clinician-rated scales, such as CGI-S A/A to assess agitation/aggression, and BEST and CGI-S to assess global improvement in BPD.

Oryzon's current objective in the short term is to submit the Ph III protocol to the FDA in H1 25 and then initiate the pivotal study subject to regulatory approval and dedicated funding. The company also plans to engage in discussions with the EMA to align the two agencies around a common clinical protocol. The estimated total sample size for the Ph III PORTICO-2 study is 350 patients (randomized 1:1), with a total trial duration of 18 weeks. Subject to FDA review of the final data, the PORTICO-2 study has the potential to be one of the two registration trials required by the FDA.

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Vafidemstat: strong cross-functional potential in neuropsychiatric disorders

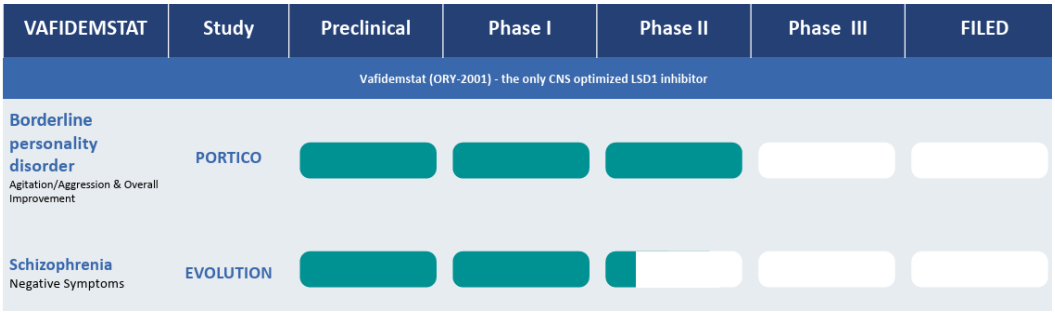
It is worth noting that, beyond BPD, vafidemstat is also being evaluated in a Ph IIb trial for the treatment of negative symptoms in schizophrenia (EVOLUTION trial) and is part of a broader approach taken by Oryzon to explore its potential in precision medicine of the central nervous system. The company is also exploring other applications in genetically defined subpopulations and neurodevelopmental disorders.

Oryzon has indeed seized the opportunity of vafidemstat's broad cross-sectional potential and is already working to demonstrate the potential of its candidate in various indications in the "mood disorders" sphere and beyond. Its most advanced trial is currently being conducted in BPD for which a pivotal Ph III trial could be initiated as early as this year, but the company has conducted trials in several other neuropsychiatric disorders and pathologies. Oryzon notably conducted two Ph IIa clinical trials to evaluate the effects of vafidemstat on agitation-aggression in patients with autism spectrum disorder, borderline personality disorder and attention deficit hyperactivity disorder (ADHD) in adults (REIMAGINE trial) and in aggressive/agitated patients with severe or moderate Alzheimer's disease (REIMAGINE-AD trial), with positive clinical results reported in both cases. Other Ph IIa trials (now completed) focused on mild to moderate Alzheimer's disease (ETHERAL study) and showed that vafidemstat leads to a significant reduction in the inflammatory biomarker YKL40 after 6 and 12 months of treatment. Another small-scale pilot trial in relapsing-remitting and secondary progressive multiple sclerosis (SATEEN study) demonstrated anti-inflammatory activity of vafidemstat. The product has also been tested in Ph II in patients with severe Covid-19 (ESCAPE trial) evaluating the drug's ability to prevent ARDS (acute respiratory distress syndrome).

The final results of the Ph IIa REIMAGINE trial were published in the journal Psychiatry and Clinical Neurosciences. This study evaluated the safety and preliminary efficacy of vafidemstat in agitation/aggression in borderline personality disorder (BPD), attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD). In work published in 2020, the product demonstrated a clinical benefit in reducing agitation/aggression in all patient populations studied. Based on these initial data, the Ph IIb PORTICO trial in BPD was conducted, with conclusive results in early 2024 on certain disease criteria. A Ph III trial is expected to be initiated this year, after the company received initial positive feedback from the FDA, with the final trial protocol to be submitted to the Agency in H1 25, with the results of this trial aiming to move towards product registration in the US and Europe under the GDP.

Currently, vafidemstat is assessed in two Phase IIb trials to evaluate its efficacy on negative symptoms and cognition in target patients:

- the PORTICO trial in BPD,
- And the EVOLUTION trial in schizophrenia.



Source: Oryzon Genomics

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Pharma's preferred strategy: technologies with multi-blockbuster potential

As we mentioned in our report published on March 3, 2025, an analysis of the evolution of M&A operations in the field of neuroscience indicates a renewed interest in the subject, particularly since 2020 as a result of the Covid-19 crisis. In our opinion, this resurgence has been motivated by two sensitive issues, particularly in the US:

- The Covid-19 crisis, which has highlighted the impact of isolation on mental health in the general population, but more specifically among those suffering from mood disorders;
- The opioid crisis facing the US, a real public health issue that calls for significant investment to address the problem of addiction and associated disorders.

We note that M&A momentum is on the rise, particularly in the CNS sector. Today, several players in the pharmaceutical industry are faced with the need to identify growth drivers with the potential to become multi-blockbusters, i.e., capable of generating revenues exceeding $10 billion, by targeting assets:

- Addressing multiple indications, a preferred strategy particularly in the I&I (immunity & inflammation) field: a single treatment to address multiple indications with common symptoms and/or underlying mechanisms (e.g., in autoimmune diseases [Sanofi's Dupixent] or metabolic diseases [Novo Nordisk's semaglutide]),
- mature products that have demonstrated robust clinical proof of concept,
- having demonstrated a strong biological rationale: understanding of the recognized, demonstrated, and validated mechanism of action,
- with robust IP: active patents in the target territories and with a sufficiently attractive exclusivity period.

Vafidemstat fits perfectly into this industrial strategy. Aggression and agitation are symptoms common to many of CNS disorders, for which vafidemstat has already shown signs of effectiveness for several of them.

Strategically strong position for M&A as a sole BPD player

After the failure of Boehringer Ingelheim (in Ph II in BPD and again recently in Ph III in schizophrenia for different candidates), Oryzon now presents itself as the only non-academic player with an active clinical program in BPD. This therefore makes it a prime target for groups wishing to integrate programs in the field of neuropsychiatric disorders into their pipeline. In addition, Oryzon's program has now reached a relatively mature stage, with a Ph III trial to be initiated this year after a refinancing anticipated in Q2 25. If the company succeeds in reproducing in Ph III in a larger cohort, the results obtained in the Ph IIb, then vafidemstat has every chance of obtaining marketing authorization from the FDA and EMA to treat BPD.

Interestingly, the two criteria that emerged as statistically significant relate to patient aggression and agitation, which correspond to very widespread symptoms common to a large number of psychiatric/psychological disorders that could potentially also be treated with vafidemstat. This offers very broad perspectives on the potential of this product, especially since the strategy of the Pharma players is precisely to develop products capable of acting on different pathologies with a cognitive component in order to target a very broad end market. This aspect is of great importance because it probably explains the increase and volumes since February, an approval of vafidemstat offering the possibility of having a multi-blockbuster product, a winning strategy adopted particularly in the field of I&I, oncology and metabolic diseases.

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Strategic plan in three phases: value inflection over the next 3-4 years

The strategy that Oryzon Genomics wishes to deploy is part of a sequence of 3 complementary objectives that can be achieved within a period of 5 years from today..

1. **Objective #1: Raise funds to launch the pivotal trial in BPD → 2025**

As stated several times, the company aims to refinance very quickly to raise the funds necessary to initiate the Ph III trial in BPD. Cash, cash equivalents and marketable securities at the end of 2024 amounted to $5.8 million. Based on the current cash burn, and without any strengthening of the cash flow since the end of 2024 (new drawdowns from the OCA line), these funds should, according to our estimates, represent a financial horizon at the end of Q2 25. However, the company should receive in the coming weeks the amount due to it as part of the European Med4Cure project financed to the tune of €1 billion. The amount to be returned to Oryzon Genomics should be between €16 and €17 million, which should extend the financing horizon by approximately 1 year, i.e. until mid-2026. It should also be remembered that the group has an OCA facility (total amount of €45m), part of which has already been exercised (nearly €24m exercised on the two OCA instruments which were set up with Nice & Green).

The Ph III PORTICO-2 trial is expected to involve 350 patients, representing a total cost of between €35 million and €40 million over a period of 3 years. At the end of February, the company held a General Meeting during which all resolutions were voted on, including some relating to financial clauses concerning, in particular, the use of OCs for a maximum possible amount of nearly €35.5 million, and refinancing of up to €100 million. In order to meet its schedule, which plans to initiate the Ph III trial by the end of the year, we anticipate a fundraising likely during Q2 25.

2. **Objective #2: Monetize Iadademstat and become a pure CNS player → 2025/27**

As mentioned in this report on p. 5 to 11, Oryzon Genomics also has business development objectives. The company's priority objective remains value creation, and this could take the form of a sale of the oncology franchise via the sell-off of iadademstat in the short/mid-term. Such an operation could represent a double interest and serve the company's strategy in the few coming years: (i) generate substantial income in the mid-term to support the development plan for vafidemstat in BPD as a priority, (ii) in order to create the best conditions for a potential takeover of the company, which would then be identified as a pure player in the CNS. We identify a favorable inflection point for such a scenario at the publication of Merck & Co's Ph III results in 2027, which could constitute a first significant jump in value within 2-3 years.

3. **Objective #3: Strengthen attractiveness as an M&A target → 2025/29**

Following the sale of iadademstat at a price we estimate to be around €450 million, Oryzon Genomics would benefit from all the resources necessary to conduct and finalize the clinical development of vafidemstat on the one hand, and to initiate developments of other assets in the CNS sphere on the other hand. With a pipeline full of several assets in the field of CNS disorders, Oryzon Genomics could be identified as a specialist in CNS disorders. Upon reaching key milestones, the main one being the final results of the Ph III PORTICO-2 in BPD, which we anticipate in 2029 (the protocol does not provide for an interim analysis but a futility analysis on a certain number of patients recruited out of the total 350 planned), Oryzon Genomics could be the subject of acquisition proposals from Pharma players. We believe that if the results of PORTICO-2 are positive and the primary endpoints prove clinically and statistically significant, they could then constitute a powerful catalyst with the potential to trigger a GO/NO GO for a takeover. In such a scenario, this would constitute a second significant jump in value over a 5-year horizon.

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Redesign of our model: updated assumptions

To take into account Oryzon Genomics' strategy in the mid-term and the changing landscape, political incentives in the neurological disorders space, the emerging strategy among large pharmaceutical groups and the privileged position that Oryzon Genomics now occupies on the M&A scene, we have redesigned our valuation model.

The main modeling assumptions include:

- a tax rate of 15% for the first two profitable years, then 25%,
- a WACC of 15%,
- a near doubling of R&D costs starting in 2026 to account for the costs associated with the Ph III trial in the BPD (we have modeled linear costs over the three-year period during which the trial will be conducted, although in reality, the costs will not be equivalent from one year to the next).

For the PORTICO program in BPD, we have selected (vafidemstat):

- Target territories: the US and the EU
- Epidemiology: 1.8% of the global population
- Vafidemstat price: €14,654 in the US and €10,467 in the EU (based on an estimate of costs borne by society in the US)
- Market share: 33% of the diagnosed and treated population
- Ph III costs: between €35 and €40 million
- Ph III launch: end of 2025
- Ph III duration: 3 years
- Final results: early 2029
- FDA marketing authorization: 2030
- Signing of an agreement: 2029 until publication of final results
- Total value of the agreement: €1.65 billion, including €50 million upfront
- Commercial exclusivity period: from 2030 to 2040 (expiration of the current patent)
- Probability of clinical success (PoS): 13.8%
- Royalty rate: 20% taking into account the de-risked stage if Ph III is successfully completed

Arguments:

- Epidemiology: A 2024 study published in the journal World Psychiatry reports that in the general adult population, the lifetime prevalence of borderline personality disorder is 0.7 to 2.7% (an average of 1.8% that we used), while its prevalence is approximately 12% in outpatient psychiatric services and 22% in inpatient psychiatric services.
- Market share: It is currently difficult to estimate the medication rate of individuals with BPD. However, it appears that the condition is undertreated, the main limitation being that there is currently no truly effective treatment for this condition. We therefore assumed a rate of 60% of diagnosed BPD individuals receiving treatment, one-third of which would be captured by vafidemstat if approved for marketing authorization. This 33% rate may seem conservative but given the nature of CNS disorders and the medication habits of these subjects, we believe it is a reasonable rate. However, it is very likely that the rate is significantly higher in subpopulations identified as being at high risk: in psychiatric hospitals and prisons (where medication is more regulated or even imposed).
- Vafidemstat pricing: According to a study published in 2019 in the journal Psychiatric Services, the social costs associated with personality disorders were estimated at between $12,696 and $19,231 per patient per year, more than double the costs associated with depression.
- PoS: Based on the success rate of a retrospective study conducted between 2011 and 2020 by BIO | QLS Advisors, we estimated a PoS for vafidemstat to reach the market of 13.8%. This may seem very conservative but given the very high failure rate in the neurological discipline, we opt for a cautious position with a PoS of Ph II at approval to integrate the real clinical risk.

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For oncology programs (iadademstat):

- Target indications: AML and SCLC
- Target areas: US and EU
- Epidemiology: Incidence of approximately 20 million cases in the US and 21 million in the EU for AML, approximately 31 million cases in the US and 45 million in the US for SCLC cancer (approximately 14% of all lung cancers)
- Target market: 40% of relapsed or resistant AML patients in the US and 50% of relapsed or refractory SCLC patients in the EU
- Iadademstat price: annual price of approximately €90k in the US and €45k in the EU
- Market share: 45% for AML, which suffers from very few alternatives, 33% for SCLC
- Reaching clinical PoC (end of Phase II) in several indications: 2027
- Agreement conclusion: 2027 upon publication of the final results of the Phase III study conducted by Merck & Co in essential thrombocythemia
- Total value of the agreement: €545m, including €20m upfront in the case of a license agreement, and €450m in the case of an asset acquisition
- Probability of clinical success (PoS): 12.6% in the license agreement scenario and 9.7% in the sell-off scenario
- Royalty rate: 10% given the intermediate stage of validated Phase II (higher costs and risks to be borne by the partner)

Arguments:

- Epidemiology: We based our analysis on Globocan data and the literature.
- Market share: We took into account the competition that exists in each indication.
- Iadademstat pricing: We based our analysis on current prices in the field of targeted therapy in hematology and rare solid cancers.
- PoS: Based on the success rate of a retrospective study conducted between 2011 and 2020 by BIO | QLS Advisors, we estimated a PoS for iadademstat to reach the market of 12.6%, which corresponds to a weighted average of the PoS in hematology and solid cancers. Regarding the divestiture scenario, we estimated a PoS of 9.7%, which corresponds to the estimated PoS of 12.6% for iadademstat to reach the market, to which we added an additional risk premium of 76.8%, which corresponds to the PoS of a Ph III in hematology. Since we assume an inflection point in 2027 through the divestment of iadademstat which could be accelerated by the Ph III results of bomedemstat expected in 2027, we partially condition the success of this scenario on the success of Merck & Co.'s Ph III trial.

Probability of clinical success by therapeutic area

Likelihood of Approval	Phase I to Approval		Phase II to Approval		Phase III to Approval		NDA/BLA to Approval	
	LOA n	Phase LOA	LOA n	Phase LOA	LOA n	Phase LOA	LOA n	Phase LOA
Hematology	352	23.9%	260	34.4%	154	71.5%	72	93.1%
Metabolic	399	15.5%	263	25.0%	114	55.7%	48	87.5%
Infectious disease	1170	13.2%	767	22.8%	353	59.4%	156	92.9%
Others	541	13.0%	387	20.5%	159	53.0%	69	88.4%
Ophthalmology	415	11.9%	327	16.6%	127	46.7%	45	91.1%
Autoimmune	1305	10.7%	892	19.3%	421	61.4%	202	94.1%
Allergy	201	10.3%	146	18.3%	54	64.7%	20	100.0%
Gastroenterology*	186	8.3%	141	17.8%	68	51.9%	33	90.9%
All indications	**12728**	**7.9%**	**8314**	**15.1%**	**3381**	**52.4%**	**1453**	**90.6%**
Respiratory	501	7.5%	322	13.5%	107	61.6%	45	95.6%
Psychiatry	442	7.3%	292	13.8%	128	51.4%	57	91.2%
Endocrine	887	6.6%	568	15.2%	275	57.1%	124	86.3%
Neurology	1411	5.9%	895	12.3%	391	46.0%	165	86.7%
Oncology	4179	5.3%	2551	10.8%	819	43.9%	324	92.0%
Cardiovascular	651	4.8%	437	9.6%	185	45.6%	80	82.5%
Urology	88	3.6%	66	8.8%	26	58.6%	13	84.6%

Figure 5b: Table likelihood of approval by disease area with corresponding n values. The n value is the total 'Advanced or Suspended' transitions of all phases used to calculate LOA. 'Phase LOA' is the probability of FDA approval for drugs from this phase of development. Source: Biomedtracker® and Pharmapremia®, 2020

Phase transition success rates by disease area

Phase Success	Phase I to II		Phase II to III		Phase III to NDA/BLA		NDA/BLA to Approval	
	n	Phase POS	n	Phase POS	n	Phase POS	n	Phase POS
Hematology	92	69.6%	106	48.1%	82	76.8%	72	93.1%
Metabolic	136	61.8%	149	45.0%	66	63.6%	48	87.5%
Infectious disease	403	57.8%	414	38.4%	197	64.0%	156	92.9%
Others	154	63.6%	228	38.6%	90	60.0%	69	88.4%
Ophthalmology	88	71.6%	200	35.5%	82	51.2%	45	91.1%
Autoimmune	413	55.2%	471	31.4%	219	65.3%	202	94.1%
Allergy	55	56.4%	92	28.3%	34	64.7%	20	100.0%
Gastroenterology	45	46.7%	73	34.2%	35	57.1%	33	90.9%
All indications	**4414**	**52.0%**	**4933**	**28.9%**	**1928**	**57.8%**	**1453**	**90.6%**
Respiratory	179	55.9%	215	21.9%	62	64.5%	45	95.6%
Psychiatry	150	52.7%	164	26.8%	71	56.3%	57	91.2%
Endocrine	319	43.3%	293	26.6%	151	66.2%	124	86.3%
Neurology	516	47.7%	504	26.8%	226	53.1%	165	86.7%
Oncology	1628	48.8%	1732	24.6%	495	47.7%	324	92.0%
Cardiovascular	214	50.0%	252	21.0%	105	55.2%	80	82.5%
Urology	22	40.9%	40	15.0%	13	69.2%	13	84.6%

Figure 2: Phase transition success rates by disease area. The n value is the total 'Advanced or Suspended' transitions of all phases used to calculate LOA. 'POS' is the probability of successfully advancing to the next phase. The ordering of disease areas is consistent with the overall likelihood of approval from Phase I, which is analyzed later in Figure 5. Source: Biomedtracker® and Pharmapremia®, 2020

Source: Clinical Development Success Rates and Contributing Factors 2011–20. BIO | QLS Advisors

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Regarding our M&A and BD assumptions, they have been detailed and supported in the chapter "Two independent franchises that could be of interest to different buyers" of this study on pages 5 to 11.

We have summarized the main financial and market access assumptions in the summary table below.

Key financial and market access assumptions

Neuropsychiatry franchise	
BPD - Licensing scenario	
NPV	**5 919**
PoS	13,8%
rNPV	**817**

From market launch to patent expiration: ISe assumptions 2030 - 2040 (m€)			
Upfront	50	3,1%	ratio upfront / milestones
Milestones	1 600	0,5%	ratio (upfront + milestones) / global sales
Sales	334 399	Licensing agreement in 2029	
Royalties	66 880	Market launch in 2030	
Total revenues Oryzon Genomics	**68 530**		

Oncology franchise	
AML + SCLC - Licensing scenario	
NPV	**192**
PoS	12,6%
rNPV	**24**

From market launch to patent expiration: ISe assumptions 2032 - 2043 (m€)			
Upfront	20	3,8%	ratio upfront / milestones
Milestones	525	3,0%	ratio (upfront + milestones) / global sales
Sales	18 152	Licensing agreement in 2027	
Royalties	1 815	Market launch in 2032	
Total revenues Oryzon Genomics	**2 360**		

Iadademstat sell off scenario	
Discounted FCF	**229**
PoS	9,7%
rNPV	**22**

ISe assumptions of an agreement in 2027 (m€)		
Upfront (one shot payment)	450	Sell off agreement in 2027
Total revenues Oryzon Genomics	**450**	

Source: Invest Securities

Valuation assumptions in the scenario of iadademstat sell off at a Ph II stage

Estimation of the agreement amount in the scenario of a iadademstat sell-off	
Imago maket capitalization before its acquisition	657 m$
Oryzon Genomics current market capitalization	218 m€
Ratio	3,014
Agreement amount for Imago's acquisition by Merck MSD	1,36 Md$
Estimated agreement for a sell-off of iadademstat over a 2-year horizon	**451 m€**

Source: Invest Securities

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Projections de ventes dans le BPD, l'AML et le SCLC (ISe)

	Borderline Personality Disorder	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
USA	Global population in US (millions)	339,5	340,1	341,8	343,5	345,2	347,0	348,7	350,4	352,2	353,9	355,7	357,5	359,3	361,1	362,9	364,7	366,5	368,4	370,2	372,0	373,9
	Prevalence	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*
	Population with BPD	6,1	6,1	6,2	6,2	6,2	6,2	6,3	6,3	6,3	6,4	6,4	6,4	6,5	6,5	6,5	6,6	6,6	6,6	6,7	6,7	6,7
	Population diagnosed and treated	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*
	Population eligible to vafidemstat	3,7	3,7	3,7	3,7	3,7	3,7	3,8	3,8	3,8	3,8	3,8	3,9	3,9	3,9	3,9	3,9	4,0	4,0	4,0	4,0	4,0
	Market shares	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%
	Penetration rate	0%	0%	0%	0%	0%	0%	0%	4%	13%	35%	65%	87%	96%	100%	100%	100%	100%	100%	100%	100%	100%
	Growth (%)									*227%*	*171%*	*87%*	*35%*	*11%*	*5%*	*0,5%*	*0,5%*	*0,5%*	*0,5%*	*0,5%*	*0,5%*	*0,5%*
	Patients under treatment	0	0	0	0	0	0	0	49 957	163 174	441 510	824 047	1 108 471	1 229 256	1 286 877	1 293 311	1 299 778	1 306 277	1 312 808	1 319 372	1 325 969	1 332 599
	Annual price per patient in US	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*	*14 654 €*
	Sales EURm (US)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**732**	**2 391**	**6 470**	**12 076**	**16 244**	**18 014**	**18 858**	**18 952**	**19 047**	**19 142**	**19 238**	**19 334**	**19 431**	**19 528**

	Borderline Personality Disorder	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
EU	Global population in EU (millions)	452,4	455,1	457,8	460,6	463,3	466,1	468,9	471,7	474,6	477,4	480,3	483,1	486,0	489,0	491,9	494,8	497,8	500,8	503,8	506,8	509,9
	Prevalence	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*	*1,80%*
	Population with BPD	8,1	8,2	8,2	8,3	8,3	8,4	8,4	8,5	8,5	8,6	8,6	8,7	8,7	8,8	8,9	8,9	9,0	9,0	9,1	9,1	9,2
	Population diagnosed and treated	*60%*	*60%*	*60%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*	*60,0%*
	Population eligible to vafidemstat	4,9	4,9	4,9	5,0	5,0	5,0	5,1	5,1	5,1	5,2	5,2	5,2	5,2	5,3	5,3	5,3	5,4	5,4	5,4	5,5	5,5
	Market shares	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%
	Penetration rate	0%	0%	0%	0%	0%	0%	0%	2%	5%	10%	13%	17%	23%	32%	45%	60%	75%	89%	100%	100%	100%
	Growth (%)									*235%*	*101%*	*31%*	*32%*	*36%*	*40%*	*41%*	*34%*	*26%*	*19%*	*13%*	*1%*	*1%*
	Patients under treatment	0	0	0	0	0	0	0	25 218	84 566	170 146	222 518	292 730	398 423	557 654	788 906	1 058 186	1 330 669	1 588 535	1 795 580	1 806 354	1 817 192
	Annual price per patient in EU	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*	*10 467 €*
	Ventes EURm (EU)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**264**	**885**	**1 781**	**2 329**	**3 064**	**4 170**	**5 837**	**8 258**	**11 076**	**13 928**	**16 627**	**18 795**	**18 907**	**19 021**

	Acute Myeloid Leukemia	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
USA	AML incidence in US ('1000)	21,2	21,6	22,0	22,3	22,7	23,1	23,5	23,9	24,3	24,7	25,1	25,6	26,0	26,4	26,9	27,3	27,8	28,3	28,8	29,3	29,8
	% relapsed/ refractory	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*
	Market penetration	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
	Patients eligible for iadademstat	2,12	2,16	2,20	2,23	2,27	2,31	2,35	2,39	2,43	2,47	2,51	2,56	2,60	2,64	2,69	2,73	2,78	2,83	2,88	2,93	2,98
	Market shares	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*
	Market penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*2%*	*5%*	*10%*	*13%*	*17%*	*23%*	*32%*	*45%*	*60%*	*75%*	*89%*	*100%*	
	Patients under treatment	0	0	0	0	0	0	0	0	0	16 683	56 556	115 034	152 087	202 264	278 303	393 787	563 177	763 668	970 813	1 171 616	1 338 801
	Annual price (US)	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*
	Sales ($)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**3**	**11**	**23**	**30**	**40**	**56**	**79**	**113**	**153**	**194**	**234**	**268**

	Acute Myeloid Leukemia	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
UE	AML incidence in EU ('1000)	23	23	24	24	24	25	25	26	26	27	27	27	28	28	29	29	30	30	31	31	32
	% relapsed/ refractory	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
	Market penetration	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
	Patients eligible for iadademstat	2,28	2,32	2,36	2,40	2,44	2,48	2,52	2,56	2,61	2,65	2,70	2,74	2,79	2,84	2,88	2,93	2,98	3,03	3,08	3,14	3,19
	Market shares	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*
	Market penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*2%*	*5%*	*10%*	*13%*	*17%*	*23%*	*32%*	*45%*	*60%*	*75%*	*89%*	*100%*	
	Patients under treatment	0	0	0	0	0	0	0	0	0	17 890	60 647	123 356	163 089	216 896	298 436	422 273	603 917	818 911	1 041 041	1 256 370	1 435 650
	Annual price (EU)	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*
	Sales (€M)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**6**	**12**	**16**	**22**	**30**	**42**	**60**	**82**	**104**	**126**	**144**

	Small Cell Lung Cancer	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
USA	Incidence cancer lung in US ('1000)	228	229	230	231	232	233	234	235	236	237	238	239	240	242	243	244	245	247	248	249	250	251
	% SCLC	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*
	Incidence SCLC in US ('1000)	32	32	32	32	33	33	33	33	33	33	33	33	34	34	34	34	34	35	35	35	35	35
	% relapsed/ refractory	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
	Patients eligible for iadademstat	21	21	21	21	21	21	21	21	22	22	22	22	22	22	22	22	22	23	23	23	23
	Market shares	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*
	Market penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*2%*	*5%*	*10%*	*13%*	*17%*	*23%*	*32%*	*45%*	*60%*	*75%*	*89%*	*100%*	
	Patients under treatment	0	0	0	0	0	0	0	0	0	107 232	359 227	722 047	943 354	1 239 785	1 685 743	2 357 108	3 331 257	4 463 884	5 607 754	6 687 808	7 551 963
	Annual price (US)	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*	*90 000*
	Sales (€M)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**29**	**98**	**197**	**257**	**338**	**460**	**643**	**909**	**1 217**	**1 529**	**1 824**	**2 060**

	Small Cell Lung Cancer	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
UE	Incidence cancer lung in EU ('1000)	321	323	324	326	327	329	331	332	334	336	337	339	341	342	344	346	348	349	351	353	355
	% SCLC	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*	*14%*
	Incidence SCLC in EU ('1000)	45	45	45	46	46	46	46	47	47	47	47	47	48	48	48	48	49	49	49	49	50
	% relapsed/ refractory	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
	Patients eligible for iadademstat	29	29	29	30	30	30	30	30	30	31	31	31	31	31	31	32	32	32	32	32	32
	Market shares	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*
	Market penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*2%*	*5%*	*10%*	*13%*	*17%*	*23%*	*32%*	*45%*	*60%*	*75%*	*89%*	*100%*	
	Patients under treatment	0	0	0	0	0	0	0	0	0	151 187	506 478	1 018 021	1 330 044	1 747 985	2 376 745	3 323 310	4 696 772	6 293 675	7 906 429	9 429 207	10 647 587
	Annual price (EU)	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*	*45 000*
	Sales (€M)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**21**	**69**	**139**	**181**	**238**	**324**	**453**	**640**	**858**	**1 078**	**1 286**	**1 452**

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Modèle de valorisation rNPV (ISe)

CNS valuation

BPD - Licensing scenario	Ph II					Ph III		Reg	Marketing											Patent expiration		
m€	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
Sales	0	0	0	0	0	0	0	996	3 276	8 251	14 405	19 308	22 184	24 695	27 210	30 123	33 070	35 865	38 129	38 338	38 549
Upfronts	0	0	0	0	0	0	50														
Milestones								100	0	0	150	0	0	250	0	300		0	400	0	400
Royalties (20%)	0	0	0	0	0	0	0	199	655	1 650	2 881	3 862	4 437	4 939	5 442	6 025	6 614	7 173	7 626	7 668	7 710
Revenues for Oryzon Genomics	0	0	0	0	0	0	50	299	655	1 650	3 031	3 862	4 437	5 189	5 442	6 325	6 614	7 173	8 026	7 668	8 110
R&D	*7*	*4*	*8*	*9*	*10*	*10*	*5*	*6*	*6*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
G&A and COGS	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*-3*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
EBITDA	-10	-7	-11	-12	-13	-14	41	290	646	1 647	3 028	3 858	4 433	5 189	5 442	6 325	6 614	7 173	8 026	7 668	8 110
Taxes	0	0	0	0	0	0	-6	-44	-161	-412	-757	-965	-1 108	-1 297	-1 360	-1 581	-1 654	-1 793	-2 006	-1 917	-2 027
FCF	-10	-7	-11	-12	-13	-14	35	247	484	1 235	2 271	2 894	3 325	3 892	4 081	4 743	4 961	5 380	6 019	5 751	6 082

Discounted FCF	**5 919**
Discount Factor (WACC)	15,1%
PoS (likehood 2025 to approval)	13,8%
rNPV	**817**

Oncology valuation

AML + SCLC - Licensing scenario	Ph II					Ph III			Reg	Marketing												
m€	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
Sales	-	-	-	-	-	-	-	-	-	55	184	371	485	639	869	1217	1722	2310	2906	3470	3923
Upfronts	-	-	-	-	20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Milestones						10			20			50		75			100		120		150
Royalties (10%)	0	0	0	0	0	0	0	0	0	5	18	37	49	64	87	122	172	231	291	347	392
Revenues for Oryzon Genomics	0	0	0	0	20	10	0	0	20	5	18	87	49	139	87	122	272	231	411	347	542
R&D	*3,5*	*1,8*	*3,8*	*4,3*	*5,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
G&A and COGS	*-3,4*	*-3,4*	*-3,4*	*-3,4*	*-3,4*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
EBITDA	-6,9	-5,3	-7,1	-7,7	11,7	10,0	0,0	0,0	20,0	5,5	18,4	87,1	48,5	138,9	86,9	121,7	272,2	231,0	410,6	347,0	542,3
Taxes	0,0	0,0	0,0	0,0	-1,7	-1,5	0,0	0,0	-3,0	-0,8	-4,6	-21,8	-12,1	-34,7	-21,7	-30,4	-68,1	-57,8	-102,6	-86,7	-135,6
FCF	-7	-5	-7	-8	10	9	0	0	17	5	14	65	36	104	65	91	204	173	308	260	407

Discounted FCF	**192**
Discount Factor (WACC)	15,1%
PoS (likehood 2025 to approval)	12,6%
rNPV	**24**

ladademstat sell off scenario																					
m€	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043
Upfront payment - sell off					450																
R&D	*3,5*	*1,8*	*3,8*	*4,3*	*5,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
G&A and COGS	*-3,4*	*-3,4*	*-3,4*	*-3,4*	*-3,4*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
EBITDA	-6,9	-5,3	-7,1	-7,7	441,7	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Taxes	0,0	0,0	0,0	0,0	-66,2	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
FCF	-7	-5	-7	-8	375	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Discounted FCF	**229**
Discount Factor (WACC)	15,1%
PoS (likehood 2025 to approval)	9,7%
rNPV	**22**

Buy recommendation reiterated, TP raised to €12.60 vs. €3.10

Benefiting from a very buoyant Momentum, Oryzon Genomics saw its share price jump during the month of February in relatively large volumes. Several extrinsic and intrinsic factors probably contributed to this rally, the main explanation being, in our opinion, that certain large US funds positioned themselves on the stock in anticipation of the upcoming launch of the Ph III trial in BPD. Given the recurring clinical failures in CNS disorders (consecutive failures of Boehringer Ingelheim in BPD and more recently in schizophrenia), in parallel with the very promising results obtained by Oryzon Genomics in Ph IIb in BPD, we believe that the market has made a valuation catch-up on the stock. Especially since the initial feedback from the FDA concerning the development plan of the pivotal Ph III in BPD, was in favor of the proposals submitted by Oryzon Genomics. The company plans to submit the pivotal trial protocol to the FDA in H1 25 with the goal of obtaining the Agency's authorization to initiate this trial before the end of H1 25. It should also be noted that in the Ph IIb trial, vafidemstat demonstrated clinically and statistically significant results in the management of aggression and agitation related to BPD. These are symptoms common to a large number of neuropsychiatric disorders, which suggests a multi-blockbuster potential for the product. And this is exactly the strategy currently being adopted by players in the field of CNS disorders: targeting an active ingredient capable of acting on cross-disciplinary aspects of neuropsychiatric disorders in order to address the largest number of patients.

Due to its mechanism of action, vafidemstat presents a versatile profile offering the opportunity of a potentially very large addressable market. This makes it a prime target for any Pharma player looking for a differentiating product with the advantage of maturity (we assume an agreement signed after the publication of the Ph III results in 2029) and therefore of being highly de-risked from a clinical perspective, which would justify a relatively substantial amount in the event of signing a licensing agreement (nearly €1.65 billion in our assumptions).

Given the potential of such an approach, we reiterate our Buy rating due to:

- the potential of vafidemstat in its target market and the broader neuropsychiatric market,
- the maturity of the program (Ph III-ready) and the results obtained in Ph IIb,
- the M&A momentum in the neuroscience field and the strong position Oryzon Genomics currently enjoys as the only player in BPD,
- and the market potential, with the current price offering an upside of more than 300% compared to our TP, which we note at €12.60 vs. €3.10 previously.

Valuation by the sum of the parts

SUM OF THE PARTS			/ per share
Neuropsychiatry (BPD)	817	(m€)	12,4 €
Oncology (AML + SCLC)	24	(m€)	0,4 €
ladademstat sell off	22	(m€)	0,3 €
Net Debt 2024	11	(m€)	0,2 €
rNPV Licensing scenario	830	(m€)	12,6 €
rNPV Sell off scenario	828	(m€)	12,6 €
Number of shares	65,8		
Price per share licensing scenario	12,6		(€)
Price per share sell off scenario	12,6		(€)
Average as our TP	12,6		(€)

Source: Invest Securities

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The main differences between the current model and the previous one lie in:

- the update of the annual treatment price in the BPD (€14,600 vs. €8,930 in the US and €10,470 vs. €5,360 in the EU),
- the modeling of the assumptions for the agreements in the CNS (total amount of €1.65 billion vs. €680 million) and in oncology (standalone strategy vs. licensing, i.e. an rNPV of €22 million to €24 million with a PoS of 9.7% to 12.6% [NPV of €192 million to €229 million] in the current assumptions vs. an rNPV of €330 million with a PoS of 25% [NPV of €1,322 million] previously),
- the adjustment of the PoS in the BPD (from 10% to 13.8%), and in oncology (from 25% to 12.6% by modeling an agreement in 2027 at the Ph II stage vs the scenario of a Ph III study to be conducted by Oryzon Genomics // sell off in 2027 with a one payment of €450m estimated on the basis of the Merck & Co / Imago benchmark: Oryzon Genomics/Imago capitalization ratio applied to the acquisition price of $1.36 billion including a PoS of 9.7% (corresponding to the PoS of 12.6% of a clinical development of iadademstat reduced by a risk premium of 76.8% linked to the chances of success of a Ph III trial in hematology that we associate with the Ph III study of Merck & Co whose results expected in 2027 could, in our opinion, constitute a trigger in read across for a repurchase of iadademstat).

Main catalysts expected in 2025:

- H1 25: Payment of the European grant for the Med4Cure project (approximately €16 million),
- H1 25: Refinancing in accordance with the resolutions passed at the last AGM,
- H1 25: FDA response for the PORTICO-2 Ph III protocol in BPD,
- June 2025: Updated results from FRIDA (EHA 2025),
- End of 2025: Launch of the pivotal Ph III trial in BPD.

Potential that goes beyond the assets currently in the clinic:

Oryzon Genomics has entered an extremely promising period. Despite recurring clinical failures in the field of CNS disorders and pathologies, stakeholders remain mobilized, as evidenced by the numerous agreements and incentives in the field that have been accelerating in recent years. In the strict field of BPD, the company is now positioned as the only player with an active clinical program. Beyond BPD, Oryzon has demonstrated the clinical potential of vafidemstat in a range of disorders such as Alzheimer's disease, schizophrenia, certain forms of autism, and attention-deficit/hyperactivity disorder. These preliminary data were recently published in the journal Psychiatry and Clinical Neurosciences, which likely also contributed to the rally at the beginning of the year. The full potential of vafidemstat is increasingly revealed through the demonstration of clinical evidence provided by Oryzon Genomics, in parallel with the scarcity of competition given the recurring clinical failures of various attempts carried out by other players including large pharmaceutical groups.

While the potential of the assets that make up the clinical pipeline is now known and recognized, it is interesting to note that Oryzon's non-clinical pipeline reveals other potentially high-value assets. Indeed, Oryzon Genomics is working on at least two other assets currently in preclinical stages, including ORY-4001, a selective HDAC6 inhibitor, for ALS (amyotrophic lateral sclerosis) and CMT (Charcot Marie-Tooth disease). This asset is particularly interesting in light of current events, the Belgian company Augustine Therapeutics having completed a private financing (Series A) of $78 million on March 24, 2025, led by the Jeito and Novo Holdings funds. The company is developing at the preclinical stage a selective inhibitor of the HDAC6 enzyme to treat neuromuscular and neurodegenerative diseases, including CMT as a first-line treatment. We believe this is a new, strong signal of interest in technologies based on epigenetics. These approaches, which involve modulating histone modifications and gene expression, are finally making their debut, with their therapeutic potential increasingly highlighted.

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FINANCIAL DATA

Share information	2019	2020	2021	2022	2023	2024e	2025e	2026e
Published EPS (€)	-0,05	-0,04	-0,06	-0,05	-0,04	-0,06	-0,04	-0,04
Adjusted EPS (€)	**-0,05**	**-0,04**	**-0,06**	**-0,05**	**-0,04**	**-0,06**	**-0,04**	**-0,04**
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Consensus EPS)	**-0,09**	**-0,07**	**-0,09**	**-0,08**	**-0,06**	**0,00**	**0,03**	**0,02**
Diff. I.S. vs Consensus	*-41,7%*	*-44,5%*	*-33,5%*	*-27,1%*	*-21,7%*	*+9558,3%*	*-231,3%*	*-262,8%*
Dividend	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Pay-out ratio	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Operating FCF	-2,68	-3,22	-4,22	-2,83	-1,49	-2,38	-0,58	-0,58
Book Value	0,89	0,81	0,88	0,87	0,95	1,14	1,35	1,32

Valuation ratios	2019	2020	2021	2022	2023	2024e	2025e	2026e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Price to Book Value	3,6x	3,6x	3,9x	2,9x	2,3x	2,7x	2,2x	2,3x
EV/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Div. yield (%)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

NB : valuation based on annual average price for past exercise

Entreprise Value (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Average number of shares (m)	68,6	93,2	80,7	77,4	77,4	65,8	64,7	64,7
Share price in €	*3,2*	*3,0*	*3,5*	*2,5*	*2,2*	*3,0*	*3,0*	*3,0*
Market cap.	220	275,8	280,4	192,3	168,5	200,3	196,9	196,9
Net Debt	-22	-26	-24	-19	2	9	-7	-8
Minorities	0	0	0	0	0	0	0	0
Provisions/ near-debt	0	0	0	0	0	0	0	0
Financial assets	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0	0
Entreprise Value (EV)	**198**	**249,8**	**256,0**	**172,9**	**171,0**	**209,4**	**190,1**	**189,2**

NB : valuation based on annual average price for past exercise

Financial ratios	2019	2020	2021	2022	2023	2024e	2025e	2026e
Adjusted EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Tax rate	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
FCF/EBITDA adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Capex/Revenue	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
WCR in % of sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
DSO (days)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROCE exc. Intangible assets	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Gearing	n.s.	n.s.	n.s.	n.s.	3,3%	12,1%	n.s.	n.s.
Net Debt/Adjusted EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Interest cover ratio	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Source : company, Invest Securities Estimates

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FINANCIAL DATA

Income statement (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Revenue	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**
Organic growth.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Adjusted EBITDA	**-3,7**	**-4,1**	**-6,9**	**-5,3**	**-4,4**	**-4,4**	**-3,5**	**-3,5**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
Adjusted depreciation	-0,1	-0,1	-0,1	-0,2	-0,2	-0,1	-0,2	-0,2
Adjusted EBITA	**-3,7**	**-4,1**	**-6,9**	**-5,3**	**-4,4**	**-4,4**	**-3,5**	**-3,5**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
Exceptional items	-0,3	0,6	0,0	0,0	0,0	0,0	0,0	0,0
EBIT	**-3,8**	**-4,3**	**-7,0**	**-5,5**	**-4,5**	**-4,4**	**-3,6**	**-3,6**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
Financial result	-0,7	-0,5	-0,2	-1,1	-1,6	-1,1	-1,6	-1,6
Profit before taxes	**-4,6**	**-4,8**	**-7,2**	**-6,6**	**-6,1**	**-5,6**	**-5,2**	**-5,2**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
Corp. tax	0,9	1,4	2,5	2,3	2,8	1,9	2,8	2,8
Minorities & affiliates	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Net attributable profit	**-3,7**	**-3,4**	**-4,7**	**-4,2**	**-3,4**	**-3,7**	**-2,4**	**-2,4**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
Adjusted net profit	**-3,7**	**-3,4**	**-4,7**	**-4,2**	**-3,4**	**-3,7**	**-2,4**	**-2,4**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***

Cash flow statement (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Adjusted EBITDA	-3,7	-4,1	-6,9	-5,3	-4,4	-4,4	-3,5	-3,5
Theoretical Tax / Adjusted EBITA	-0,3	-0,3	-0,4	-0,5	-0,6	-0,4	-0,8	-0,8
Capex	-0,3	0,6	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF bef. WCR	**-4,2**	**-3,9**	**-7,2**	**-5,8**	**-5,0**	**-4,8**	**-4,3**	**-4,3**
Change in WCR	0,3	-1,2	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF	**-4,0**	**-5,1**	**-7,2**	**-5,8**	**-5,0**	**-4,8**	**-4,3**	**-4,3**
Acquisitions/disposals	-9,6	-9,1	0,0	0,0	0,0	-10,4	0,0	0,0
Capital increase/decrease	14,3	18,4	-0,2	-1,1	10,0	5,0	15,0	-1,6
Dividends paid	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Other adjustments	-1,2	-1,6	2,6	1,5	0,9	1,2	1,5	1,5
Published Cash-Flow	**-0,5**	**2,6**	**-4,8**	**-5,4**	**5,8**	**-9,0**	**12,2**	**-4,4**

Balance Sheet (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Assets	42,4	51,7	62,2	77,7	91,8	99,1	113,9	131,0
- of which Intangible assets/GW	39,9	49,2	59,7	75,2	89,2	96,5	111,4	128,5
- of which tangible assets	0,6	0,6	0,6	0,6	0,6	0,6	0,6	0,6
WCR	-3,1	-1,9	-1,9	-1,9	-1,9	-1,9	-1,9	-1,9
- of which trade receivables	2,1	2,4	2,4	2,4	2,4	2,4	2,4	2,4
- of which inventories	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3
Group equity capital	61,1	75,9	71,2	67,0	73,7	75,0	87,6	85,1
Minority shareholders	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Provisions	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Net financial debt	**-21,9**	**-26,1**	**-24,4**	**-19,5**	**2,5**	**9,0**	**-6,8**	**-7,7**
- of which gross financial debt	13,2	13,5	13,4	16,0	16,0	16,0	16,0	14,4
- of which gross cash	35,1	39,6	37,8	35,4	13,5	6,9	22,8	22,1

Source : company, Invest Securities Estimates

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ORYZON GENOMICS

INVESTMENT CASE

ORYZON GENOMICS is a Spanish biotechnology company specializing in the treatment of neurodegenerative diseases and cancer. Specializing in the field of epigenetics, the company aims, in all of its development programs, to identify biomarkers through its genetic and proteomic platforms in order to develop small molecule drugs. The company has delivered interesting results with its most advanced programs in areas more or less invested in terms of overall R&D efforts, cancer but also Covid-19 and cognitive disorders associated with neurodegenerative diseases or disorders of the personality.

SWOT ANALYSIS

STRENGHTS

- Epigenetic platform
- Extensive development pipeline
- Differentiating positioning

WEAKNESSES

- No partnership
- Risky indications (CNS)
- Intense competition in oncology

OPPORTUNITIES

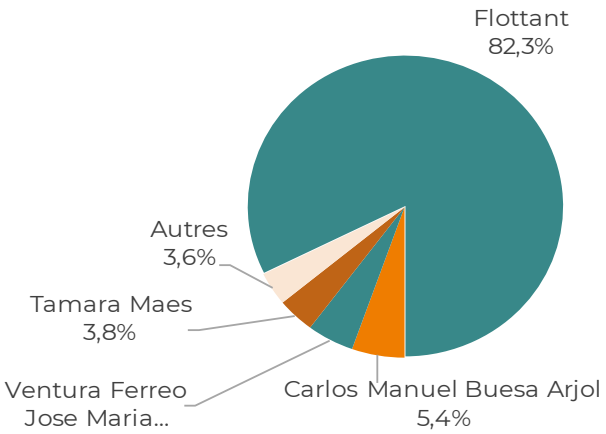
- Potential partnership
- Extension of indications

THREATS

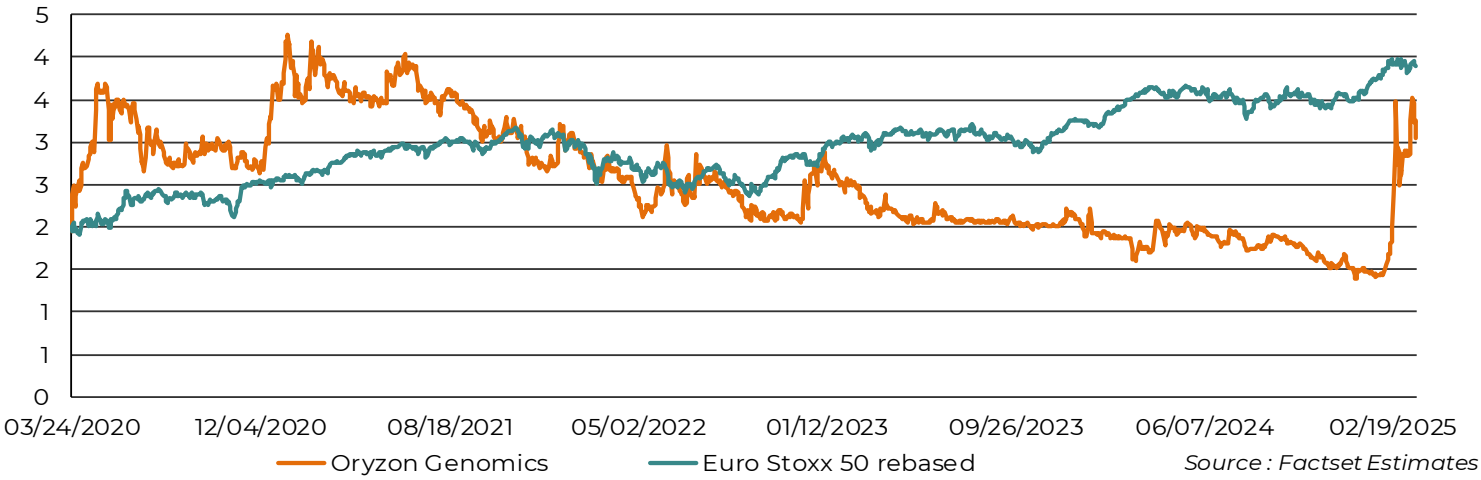
- Clinical and regulatory risk
- Commercial risks
- Legal risks

ADDITIONAL INFORMATION

Shareholders



SHARE PRICE CHANGE FOR 5 YEARS



Source : Factset Estimates

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TARGET PRICE AND RECOMMENDATION

Our analyst ratings are dependent on the expected absolute performance of the stock on a 6- to 12-month horizon. They are based on the company’s risk profile and the target price set by the analyst, which takes into account exogenous factors related to the market environment that may vary considerably. The Invest Securities analysis office sets target prices based on a multi-criteria fundamental analysis, including, but not limited to, discounted cash flows, comparisons based on peer companies or transaction multiples, sum-of-the-parts value, restated net asset value, discounted dividends.

Ratings assigned by the Invest Securities analysis office are defined as follows:

- BUY: Upside potential of more than 10% (the minimum upside required may be revised upward depending on the company’s risk profile)
- NEUTRAL: Between -10% downside and +10% upside potential (the maximum required may be revised upward depending on the company’s risk profile)
- SELL: Downside potential of more than 10%
- TENDER or DO NOT TENDER: Recommendations used when a public offer has been made for the issuer (takeover bid, public exchange offer, squeeze-out, etc.)
- SUBSCRIBE or DO NOT SUBSCRIBE: Recommendations used when a company is raising capital
- UNDER REVIEW: Temporary recommendation used when an exceptional event that has a substantial impact on the company’s results or our target price makes it impossible to assign a BUY, NEUTRAL or SELL rating to a stock

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12-MONTH HISTORY OF OPINION

The table below reflects the history of price recommendation and target changes made by the financial analysis office of Invest Securities over the past 12 months.

Company Name	Main Author	Release Date	Rating	Target Price	Current Share price	Potential
Oryzon Genomics	Jamila El Bougrini	17-janv.-25	ACHAT	3,1	1,5	+112%

DETECTION OF CONFLICTS OF INTEREST

	Oryzon Genomics
Invest Securities was lead manager or co-lead manager in a public offer concerning the financial instruments of this issuer during the last twelve months.	No
Invest Securities has signed a liquidity contract with the issuer.	No
Invest Securities and the issuer have signed a research service agreement.	Yes
Invest Securities and the issuer have signed a Listing Sponsor agreement.	No
Invest Securities has been remunerated by this issuer in exchange for the provision of other investment services during the last twelve months (RTO, Execution on behalf of third parties, advice, placement, underwriting).	No
This document was sent to the issuer prior to its publication. This rereading did not lead the analyst to modify the valuation.	No
This document was sent to the issuer for review prior to its publication. This rereading led the analyst to modify the valuation.	No
The financial analyst has an interest in the capital of the issuer.	No
The financial analyst acquired equity securities of the issuer prior to the public offering transaction.	No
The financial analyst receives remuneration directly linked to the transaction or to an investment service provided by Invest Securities.	No
An executive officer of Invest Securities is in a conflict of interest with the issuer and was given access to this document prior to its completion.	No
Invest Securities or the All Invest group owns or controls 5% or more of the share capital issued by the issuer.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net long position of more than 0.5% of the issuer's capital.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net short position of more than 0.5% of the issuer's capital.	No
The issuer owns or controls 5% or more of the capital of Invest Securities or the All Invest group.	No

Invest Securities's conflict of interest management policy is available on the Invest Securities website in the Complicance section. A list of all recommendations released over 12 months as well as the quarterly publication of "BUY, SELL, NEUTRAL, OTHERS" over 12 months, are available on the Invest Securities research platform.

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